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Comparison of the Cellularity and Presence of Residual Leukemia in Bone Marrow Aspirate and Biopsy Specimens in Pediatric Patients With Acute Lymphoblastic Leukemia (ALL) at Day 7–14 of Chemotherapy

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Background. Many pediatric chemotherapy protocols for treatment of ALL require a bone marrow examination at day 7 or day 14 after initiation of therapy. The usefulness of a bone marrow biopsy, in addition to an aspirate, has been a frequently asked question.

Procedure. This study addresses the evaluation of bone marrow cellularity and presence of residual leukemia in both aspirate and biopsy specimens in 45 consecutive pediatric patients (ages 1–19 years, 19 females, and 26 males) with ALL 7–14 days after initiation of therapy.

Discussion. 20/45 patients showed evidence of residual leukemia by bone marrow biopsy; 16/20 (80%) of these had evidence of residual leukemia in the aspirate specimen. Of the 4 aspirate specimens that did not demonstrate residual leukemia, 2 had <5% blasts and 2 had too few cells in the aspirate for evaluation. Of the 25/45 bone marrow biopsy specimens with no detectable residual leukemia, 14 of the aspirates had <5% blasts, and 11 had too few cells in the aspirate for evaluation. 13/45 (29%) of the aspirates had too few cells for a differential count. The bone marrow cellularity judged from the aspirate specimen was considered to be low (0–1+) in 34/45 patients. Of these 34 patients, the bone marrow biopsy showed hypocellularity (<20% cellularity) in 12/34, moderate cellularity (20–79% cellularity) in 14/34, and hypercellularity (>79% cellularity) in 8/34.

Conclusions. We conclude that both the bone marrow aspirate and biopsy specimens provide important information in evaluating the response to chemotherapy in pediatric patients with ALL at day 7–14 of induction chemotherapy. The aspirate alone may be misleading in terms of cellularity in many patients and may not provide evidence of residual leukemia. Med. Pediatr. Oncol. 29:541–543, 1997.

Key words: ALL; acute leukemia; bone marrow aspirate; bone marrow biopsy

INTRODUCTION

Bone marrow blast percentage is used frequently in assessing the early response of patients with acute leukemia to chemotherapy. In many multicenter trials, the percentage of blasts in a bone marrow aspirate at day 7 or day 14 of induction chemotherapy is used to decide subsequent chemotherapy [1]. At this time, pancytopenia and bone marrow hypocellularity are commonly seen.

Bone marrow aspirates provide excellent morphology of the cells in the bone marrow, but are less helpful than bone marrow biopsies or clot sections in providing a representative estimate of cellularity. Previous studies in pediatric and adult patients have come to different conclusions as to the necessity of a bone marrow biopsy in assessing cellularity [2,3,4,5]. Some have suggested that the bone marrow aspirate particle preparation may be a good or adequate substitute for a bone marrow biopsy [6]. However, none of these studies have looked specifically at the problematic day 7 or day 14 of induction chemotherapy bone marrow specimens where insufficient aspirate may be available for particle sections.

In this study, we address the question of whether a bone marrow biopsy is necessary, in addition to an aspirate, at day 7 or 14 in pediatric patients receiving induction chemotherapy for acute lymphoblastic leukemia (ALL).

METHODS

Bone marrow specimens in which both an aspirate and biopsy were performed were evaluated in 45 consecutive pediatric patients with ALL 7–14 days after initiation of induction chemotherapy. The bone marrow aspiration and biopsy were performed in the posterior iliac crest using a Jamshidi ® disposable Illinois sternal/iliac 15 gauge aspiration needle and Jamshidi ® 11 gauge disposable bone marrow biopsy/aspiration needle, respectively.

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TABLE I. Presence of Leukemia as Assessed in Bone Marrow Aspirates and Bone Marrow Biopsies Performed at the Same Time

	Biopsy		
Aspirate	Positive	Negative	Total
Positive	16	0	16
Negative	2	14	16
Too few cells to count	2	11	13
Total	20	25	45

TABLE II. Estimate of Cellularity of Aspirate as Compared to Biopsy

	Biopsy			
Aspirate	Hypocellular <20%	Moderately cellular 20–79%	Hypercellular ⩾80%	Total
0−+	12	14	8	34
++	1	3	1	5
+++	0	4	2	6
Total	13	21	11	45

Depending on the physician's preference, either the aspiration or the biopsy was performed first. However, the two needles were angled in different directions. The procedure used was similar to that described by Jamshidi and Swaim [7]. Aspirate smears were prepared at the bedside and were stained with Wright stain in the laboratory. The biopsy was immediately fixed in Zenker Solution for 24 hours or 10% buffered formalin, followed by routine histologic processing and staining with hematoxylin and eosin. Since the aspirate was so scanty in many patients, and there was insufficient material available for clot sections, this was not routinely performed.

Assessment of the percentage of blasts and the cellularity were made on the aspirate and the biopsy. If sufficient cells were present in the aspirate, a 200 cell differential was performed on the aspirate specimens, and the percentage of blasts recorded. Cellularity of the aspirates was graded 0–3+. In the biopsy, the presence or absence of clusters of immature cells was noted, and the percentage of cellularity was recorded. For purposes of grouping, the biopsies were considered hypocellular with <20% cellularity, moderately cellular with 20–79% cellularity, and hypercellular with >79% cellularity.

RESULTS

Of the 45 consecutive pediatric patients with ALL in whom both a bone marrow aspirate and biopsy were available for evaluation at day 7–14 of induction chemotherapy, 43 were receiving initial induction chemotherapy and 2 were being treated for bone marrow relapse. The patients ranged in age from 1–19 years (mean age 7.5 years). There were 19 females and 26 males. Thirty-eight day 7 marrows and seven day 14 marrows were evaluated; there did not appear to be any observable differences in the day 7 and day 14 marrows.

Twenty of the 45 patients had evidence of residual leukemia in the bone marrow biopsy (either focal collections or diffuse effacement of the bone marrow by immature cells). Sixteen of these 20 patients (80%) also had evidence of residual leukemia in the aspirate with more than 5% blasts (range: 7–100% blasts) (Table I). Of the 4 aspirate specimens that did not demonstrate residual leukemia, 2 had an evaluable aspirate with <5% blasts and 2 had too few cells in the aspirate for evaluation.

Of the 25/45 bone marrow biopsies with no detectable leukemia, 14 of the aspirates had <5% blasts, and 11 had too few cells in the aspirate for evaluation. Thus, there were no aspirates that showed residual leukemia when the biopsy was negative for residual leukemia. Of note, 13/45 (29%) of the aspirates overall had too few cells for evaluation.

With regard to bone marrow cellularity assessment, the cellularity in the aspirate was judged to be low (0–1+) in 34/45 patients (Table II). Of these 34 patients, the bone marrow biopsy was hypocellular (<20% cellularity) in 12/34, moderately cellular (20–79% cellularity) in 14/34, and hypercellular (>79% cellularity) in 8/34. Of the 11 patients in whom aspirate cellularity was found to be moderate to high (2–3+), the bone marrow biopsy cellularity also was evaluated as moderately cellular to hypercellular (20–100% cellularity) in 10/11.

DISCUSSION

In many treatment protocols for pediatric patients with ALL, the percentage of blasts in the bone marrow obtained at day 7 or day 14 of induction chemotherapy is used to make therapeutic decisions [1]. This study was undertaken to see whether an aspirate specimen alone could be reliably used for that assessment or whether it was necessary also to perform a bone marrow biopsy.

In almost one-third of the specimens (29%), the bone marrow aspirate had too few cells for evaluation. In the 18 specimens with an evaluable aspirate that had evidence of residual leukemia in the biopsy, 16 showed residual leukemia in the aspirate also (88%); in 2 patients (12%) with an evaluable bone marrow aspirate, residual leukemia would have been missed. An additional 2 patients in whom the aspirate was too scanty to be evaluated had evidence of residual leukemia in the biopsy. Therefore, 4/20 (20%) of patients would have had residual leukemia missed had only an aspirate been performed. Our study included 38 day 7 marrows and 7 day 14 marrows. We did not observe any difference in the day 7 and day 14 marrows with regard to correlation of percentage of blasts or cellularity, but the numbers are too small to draw a definite conclusion.

As has been described previously [2], the bone marrow biopsy was found to be a better specimen in which to judge cellularity than the aspirate. In the 34 patients in our study in whom the aspirate had low cellularity (0–1+ cellularity), 12 were hypocellular in the biopsy (<20% cellularity), 14 were moderately cellular (20–79% cellularity), and 8 were hypercellular (>79% cellularity). Therefore, the cellularity would have been underestimated in 22/34 patients (65%).

A recent study in children with newly diagnosed ALL evaluated the significance of the bone marrow biopsy findings in the day 7 assessment of patients with ALL who were in remission at day 28 [8]. They found that the percentage of blasts in the biopsy was generally higher than in the aspirate and that there was little correlation between the cellularity of the bone marrow biopsy and the percentage of leukemic blasts in the aspirate.

The authors created the ''absolute blast index'', which is the product of the biopsy cellularity and either the percentage of blasts in the biopsy or in the aspirate. It was demonstrated that the ''absolute blast index'' at day 7 in patients who achieved a complete remission by day 28 was highly predictive of relapse-free survival, and therefore it was concluded that both an aspirate and biopsy should be performed at day 7 as valuable prognostic information will be gained.

CONCLUSION

Based upon the results of our study, and supported by the data reported by Schultz et al. [8], a bone marrow biopsy in addition to a bone marrow aspirate, should be performed in children with ALL at induction day 7–14 examinations. Our findings suggest that the bone marrow biopsy provides additional sensitivity in detecting residual leukemia in the day 7–14 bone marrow examination that may not be provided in the bone marrow aspirate alone. However, it would be useful to have both bone marrow aspirates and biopsies performed in large multi-institution clinical trials with long-term follow-up to adequately assess the relative importance of information obtained from the aspirate and the biopsy. The difference in findings, both in percentage of blasts and cellularity, between the aspirate and biopsy also points out the need for protocols in multi-institution studies to be explicit in the type of bone marrow specimen being evaluated at different time points, since the information obtained from these two methods may be different.

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